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GENERAL HOSPITAL PSYCHIATRY

The relationship between chronic physical conditions, multimorbidity and anxiety in the general population: A global perspective across 42 countries

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Abstract

Objective

This cross-sectional study assessed the association of chronic physical conditions and multimorbidity with anxiety among community-dwelling adults in 42 countries.

Method

Data were analyzed from the World Health Survey including 181,845 adults aged ≥18 years. Anxiety in the past 30 days and nine chronic physical conditions (angina, arthritis, asthma, chronic back pain, diabetes, edentulism, hearing problem, tuberculosis, and visual impairment) were assessed. Multivariable logistic regression analyses were conducted to explore the associations between chronic physical conditions or the number of them and anxiety.

Results

After adjustment for confounders, most of the individual chronic physical conditions were significantly associated with anxiety. Compared to those with no physical health conditions, one condition was associated with an almost twofold increased odds of anxiety symptoms (OR=1.94; 95%CI=1.76-2.13), while this figure rose to 5.49 (3.73-8.09) in those with ≥5 conditions.

Conclusions

Our data suggest that increasing numbers of chronic physical conditions are associated with higher odds for anxiety. Health care providers should consider the presence of anxiety symptoms especially in individuals with physical multimorbidity.

Keywords: anxiety, multimorbidity, angina, asthma, back pain, arthritis

Introduction

Anxiety is a common and disabling mental health condition [1]. It can greatly impair a person's functioning, quality of life and well-being [2]. Anxiety is characterized by excessive and persistent (yet often unrealistic) worry which can inhibit one's ability to carry out activities of daily living, and which, if left untreated can develop into an anxiety disorder [3]. In a systematic review of prevalence studies across 44 countries, the global point prevalence of anxiety disorders was estimated at 7.3% (95% confidence interval, CI=4.8-10.9), suggesting that one in 14 people around the world at any given time has an anxiety disorder, while roughly one in nine (11.6%, 95% CI=7.6-17.7) has an anxiety disorder in any given year [4]. Anxiety disorders are the sixth leading global cause of years lived with disability [5]. Moreover, the global financial burden of anxiety is substantial, owing to lost work productivity and high medical resource use [6, 7].

There is growing recognition that numerous mental health conditions are associated with an increased physical health burden. For example, it is well established that anxiety is associated with several chronic physical co-morbidities [1]. Of particular concern are cardiovascular diseases [8], diabetes [9], pulmonary diseases [10], chronic pain [11], infectious diseases such as tuberculosis [12], arthritis [13], edentulism [14], and mainly in older people, visual impairment [15] and hearing problems [16]. Given the increasing prevalence of chronic conditions worldwide [17], a further understanding of the determinants, consequences and management of the comorbidity between anxiety and chronic physical conditions should be a research priority. Whilst progress has been made, most studies to date have however, examined the co-occurrence of anxiety with a single comorbid physical health condition. For example, in a recent cross-sectional household survey of community-dwelling adults conducted in 17 countries (47,609 participants) [18], 9 out of the 10 investigated

chronic physical health conditions (only the risk for cancer was not increased) were associated with higher odds for generalized anxiety disorder with odds ratios (OR) ranging from 1.3 (95% CI=1.0-1.6) for diabetes to 2.5 (95% CI=1.8-3.5) for a chronic lung disease.

Whilst investigating single chronic conditions is important, there is increasing recognition that many people may have multiple comorbidities. Multimorbidity (i.e. the presence of multiple chronic conditions) is relatively common in the general population with reported prevalence figures as high as 72% [19]. The heightened prevalence of multimorbidity is mainly due to the growing incidence of chronic conditions [17] and increasing life-expectancies, and it is undoubtedly one of the most significant challenges faced by health care providers and governments across the globe [20, 21]. Multimorbidity is associated with a marked lower quality of life [22], increased health-care utilization [23], and ultimately, a higher risk for premature mortality [24]. Despite this, there is a paucity of studies on the associations between anxiety and multimorbidity. Only one population study to date among 4219 participants 65 years or older in the US [25] found that two and ≥ three medical conditions yielded a 1.96-fold (95% CI=1.13–3.41) and 3.49-fold (95% CI=2.05–5.95) increased odds of elevated anxiety respectively, compared to those with no medical conditions. Whilst helpful, the relatively modest sample size, restriction to a single country and focus only on older adults, limits the generalizability of the findings. Thus, more research on the prevalence of anxiety in people with multimorbidity, in particular across increasing number of co-morbidities, is essential to identify high risk subgroups, which would preferentially benefit from tailored preventative and therapeutic strategies.

To the best of our knowledge, there are no multinational representative population studies investigating associations between anxiety and multimorbidity. This is an important research gap, given the increasing prevalence of chronic physical health conditions globally, and especially in low- and middle-income countries [26]. Understanding associations

between multimorbidity and anxiety can inform the development of targeted interventions and policies. The aim of the current study therefore was to explore the association between anxiety, chronic conditions and multimorbidity across 42 countries from Africa, Asia, Europe, and Latin-America, and to assess whether the associations are similar across all countries.

Methods

Procedure and settings

The current paper utilized data from the World Health Survey (WHS), a cross-sectional study undertaken in 2002-2004 in 70 countries worldwide. Data were collected using single-stage random sampling and stratified multi-stage random cluster sampling across 10 and 60 countries respectively. Full details of the WHS are freely available elsewhere (http://www.who.int/healthinfo/survey/en/). Briefly, persons aged ≥18 years with a valid home address were eligible to participate. Each member of the household had equal probability of being selected by utilizing Kish tables. A standardized questionnaire, translated accordingly, was used across all countries. The individual response rate (i.e. ratio of completed interviews among selected respondents after excluding ineligible respondents from the denominator) ranged from 63% (Israel) to 99% (Philippines) [27]. In order to conduct the study, ethical approval was obtained from the ethical boards at each study site. Sampling weights were generated to adjust for non-response and the population distribution reported by the United Nations Statistical Division. Informed consent was obtained from all participants.

Anxiety (outcome variable)

Anxiety was assessed by the question 'Overall in the past 30 days, how much of a problem did you have with worry or anxiety' with response alternatives: none, mild, moderate, severe, and extreme. In accordance with previous WHS publications, those who answered severe and extreme were considered to have anxiety [28, 29].

Chronic physical conditions and numbers of chronic physical conditions (exposure variables)

A total of nine physical conditions were assessed as part of the WHS. Arthritis, asthma, and diabetes were based on self-reported lifetime diagnosis. For angina, in addition to a self-reported diagnosis, a symptom-based diagnosis based on the Rose questionnaire was also used [30]. Chronic back pain was defined as having had back pain (including disc problems) every day during the last 30 days. Visual impairment was defined as having extreme difficulty in seeing and recognizing a person that the participant knows across the road (i.e., from a distance about 20 meters) [31]. A validity study showed that this response likely corresponds to World Health Organization definitions of visual impairment [31]. The participant was considered to have hearing problems if the interviewer observed this condition at the end of the survey. Edentulism was assessed by the question "Have you lost all your natural teeth?" Those who responded affirmatively were considered to have edentulism. Finally, a tuberculosis diagnosis was based on past 12-month symptoms and was defined as: 1) having had a cough that lasted for three weeks or longer; and 2) having had blood in phlegm or coughed up blood [32]. We calculated the total number of these conditions while allowing for one missing variable in order to retain a larger sample size. The number of chronic physical conditions was categorized as 0, 1, 2, 3, 4, and ≥5.

Co-variates

The selection of the co-variates was based on past literature and included sex, age (18-34, 35-59, ≥60), wealth, and depression [25]. Principal component analysis based on 15-20 assets was conducted to establish country-wise wealth quintiles. Past 12-month depression was defined using the DSM-IV algorithm using individual questions of the World Mental Health Survey version of the Mental Health Composite International Diagnostic Interview (CIDI) [33], and was based on duration and persistence of depressive symptoms in the past 12 months using the same algorithms as previous WHS publications [34, 35]. Respondents were

first asked five questions. Those who answered 'Yes' to four of them were considered as possibly having depression or a major depressive episode. Specifically, respondents were asked: "During the last 12 months have you ever experienced…": (a) A period lasting several days when you felt sad, empty or depressed? (b) A period lasting several days when you lost interest in most things you usually enjoy such as hobbies, personal relationships or work? (c) A period lasting several days when you have been feeling your energy level decreased or that you were tired all the time? (d) Did you lose your appetite? (e) Did you notice any slowing down in your thinking?'. Among those with possible depression, individuals who further responded 'Yes' to both of the following questions were classified as having depression: (a) Was this period for more than 2 weeks? (b) Was this period most of the day, nearly every day?

Statistical analysis

Of the 70 countries which participated in the WHS, 69 had data which is publically available. Ten countries (Austria, Belgium, Denmark, Germany, Greece, Guatemala, Italy, Netherlands, Slovenia, and UK) were excluded due to lack of data on sampling information. A further 9 countries (Finland, France, Ireland, Israel, Luxembourg, Morocco, Norway, Portugal, Sweden) were deleted as data on anxiety and/or some of the chronic physical conditions were not collected. Turkey was also dropped due to a lack of information on depression. Furthermore, 5 countries (Congo, Mali, Mexico, Slovakia, Swaziland) with more than 25% of data on the number of chronic physical conditions and/or anxiety missing were also deleted. Finally, Kazakhstan and Sri Lanka were deleted due to their exceptionally high prevalence of anxiety (79.2% and 65.2% respectively). Thus, the final sample consisted of 42 countries (n=181,845). These data were nationally representative in all countries with the exception of

China, Comoros, Ivory Coast, India, and Russia where the study was conducted in geographically restricted areas.

The statistical analysis was done with Stata 14.1 (Stata Corp LP, College station, Texas). Descriptive analyses were conducted to characterize the study sample. The difference in sample characteristics by the presence of anxiety was tested by Chi-squared tests. Tetrachoric correlations between each pair of physical health condition were calculated for those with anxiety. Using the sample including all countries, multivariable logistic regression analysis was performed to assess the associations of each chronic physical condition and number of chronic physical conditions (exposure variables) with anxiety (outcome variable). Separate models were constructed for each chronic physical condition and number of chronic physical conditions. Two models were constructed: Model 1 - adjusted for sex, age, wealth, and country; Model 2 - adjusted for the variables in Model 1 and depression. We also constructed models adjusting for depression as a previous World Mental Health Survey study [36], demonstrated that the risk for various chronic conditions is higher in those with comorbid depressive–anxiety disorder than depression or anxiety alone. To adjust for country, dummy variables for each country were included in the models, following the methods used in previous WHS publications [37, 38]. The number of chronic physical conditions was included in the models as a categorical variable in this analysis.

We also conducted country-wise multivariable logistic regression analyses to assess the association between the number of chronic physical conditions and anxiety while adjusting for sex, age, wealth, and depression. Given that there was a linear increase in the odds for anxiety with increasing numbers of chronic physical conditions in the above-mentioned pooled multivariable analysis, we included the number of chronic physical conditions as a continuous variable in the country-wise models. A pooled estimate was obtained by combining the estimates for each country into a random-effect meta-analysis. To

assess the level of between-country heterogeneity in the association between the number of chronic physical conditions and anxiety, the Higgins' I^2 statistic was calculated. This represents the degree of heterogeneity that is not explained by sampling error with a value of <40% often considered as negligible and 40-60% as moderate heterogeneity [39]. The sample weighting and the complex study design were taken into account in all regression analyses as well as the calculation of proportions and their 95% CIs. Results from the logistic regression models are presented as ORs with 95% CIs. The level of statistical significance was set at $P<0.05$.

Results

The mean age (SD) of the sample was 38.6 (16.1) years and 50.6% were females. The overall prevalence of anxiety was 10.3%. The prevalence of chronic physical conditions ranged from 1.4% (visual impairment) to 15.1% (angina) (**Table 1**). More than one-third of the sample had at least one chronic physical condition and 13.4% had multimorbidity. Female sex, older age, lower levels of wealth, depression, all chronic physical conditions, and higher numbers of chronic physical conditions were associated with higher prevalence of anxiety. The prevalence of anxiety was much higher for all chronic physical conditions compared to the overall prevalence (10.3%) with the highest prevalence being observed for visual impairment (43.4%), chronic back pain (28.6%), and tuberculosis (24.7%) (**Figure 1**). There was a linear increase in the prevalence of anxiety with increasing numbers of chronic physical conditions where this prevalence increased from 13.8% for only one chronic physical condition to 47.3% with ≥5 conditions. The correlations between the chronic physical conditions are shown in **Table 2**. The strongest correlations were observed for: arthritis and angina or chronic back pain; hearing problem and edentulism or visual impairment. The associations between chronic physical conditions or their numbers and anxiety estimated by multivariable logistic regression are shown in **Table 3**. In the models unadjusted for depression, the OR of the individual chronic physical conditions and the number of them were significant in all models with the OR ranging from 1.14 (edentulism) to 4.12 (visual impairment) for the individual conditions. After adjustment for depression, the ORs were attenuated but still

remained significant for all chronic physical conditions and the number of them with the exception of edentulism. The significant ORs for the individual conditions ranged from 1.50 (hearing problem) to 3.69 (visual impairment), while compared to those with no chronic physical condition, there was a linear increase in the ORs associated with increased number of conditions: 1 condition (OR=1.94; 95%CI=1.76-2.13), 2 conditions (OR=2.63; 95%CI=2.34-2.96); 3 conditions (OR=3.56; 95%CI=3.00-4.22); 4 conditions (OR=4.69; 95%CI=3.64-6.04); and ≥5 conditions (OR=5.49; 95%CI=3.73-8.09). The country-wise association between the number of chronic physical conditions and anxiety estimated by multivariable logistic regression is shown in **Figure 2**. The ORs associated with a one-unit increase in the number of chronic physical conditions ranged from 1.24 in Ecuador to 2.82 in China with the pooled OR (95%CI) estimated by meta-analysis being 1.54 (1.48-1.59). The ORs were significant in all countries with the exception of Bosnia-Herzegovina. A moderate level of between-country heterogeneity was observed (Higgin's I^2= 42.2).

Discussion

General findings

To the best of our knowledge, this is the first multinational study to explore associations between chronic conditions, multimorbidity and anxiety. While one in ten reported being worried or anxious in the past 30 days, more than one-third of the sample had at least one chronic physical condition and 13.4% suffered from multimorbidity (i.e. at least 2 chronic physical conditions). The findings were consistent across all countries. Our data show that the ubiquity of multiple chronic conditions likely compounds the higher odds of anxiety symptoms. There was a linear increase in the prevalence of anxiety with increasing numbers of chronic physical conditions where the prevalence increased from 13.8% for only one chronic physical condition to 47.3% with ≥5 conditions. In the adjusted logistic regression, the presence of one physical comorbidity was associated with an almost 2-fold increased odds of anxiety symptoms (OR 1.94), rising to an OR of 5.49 in those with 5 or more conditions. Our data also show that the prevalence of anxiety is much higher for all chronic physical conditions than people without the condition. This finding suggests that anxiety symptoms are associated with the dysregulation of multiple physiological systems and is not limited to respiratory, cardiovascular, metabolic, and inflammatory systems. The inclusion of depression in the models led to an attenuation of the associations for all chronic conditions. Higher numbers of chronic conditions were strongly and significantly associated with anxiety even after adjustment for depression.

One should note that our data are cross-sectional and we therefore cannot make inference to the directionality of our findings. However, a number of hypotheses have been proposed for the increased risk of physical conditions in people with anxiety including psychotropic medication use [40], biological risk factors such as an increased inflammatory profile, including increased levels of C-reactive protein and interleukin-6 [41] and

hypothalamic-pituitary-adrenocortical (HPA) axis dysregulation [42]. Moreover, a stress response may contribute to the pathophysiology of both, anxiety and several chronic conditions [43]. The heightened presence of anxiety among people with several chronic conditions and especially those with multimorbidity may in turn be related to the associated worry of having an illness and be attributed to difficulty adjusting to the burden of the illnesses [44]. Alternatively, another possible explanation for the association is that those who already have anxiety symptoms may receive more medical diagnoses if these symptoms result in patients visiting their doctors more often [25]. Additionally, anxious persons may be more attentive of bodily symptoms, thus leading to more diagnoses [25]. Finally, feelings of anxiety may also lead to unhealthy behaviors, such as smoking [45], alcohol consumption [46], and a sedentary lifestyle [47], which might also be implicated in the development of chronic conditions and multimorbidity.

Practical implications

Given the early onset of anxiety and the similarly early etio-pathogenesis of many chronic physical conditions [50], treatment of anxiety should optimally incorporate attention to preventing the development of other chronic diseases and multimorbidity by focusing on healthy lifestyle behaviors, with a parallel focus on anxiety symptoms emerging early in the course of the treatment for chronic physical conditions. Much could be done in primary health care settings to optimize chronic disease prevention approaches for those with mental health symptoms and a mental health focus in those with chronic conditions. Optimal primary prevention of chronic physical conditions among people with anxiety (and vice versa) could enhance the quality of life of many people worldwide.

Limitations and future research

As stated, the most important limitation of the current study is its cross-sectional nature which limits conclusions about the direction or causal nature of the relationships between the presence of anxiety, chronic conditions and multimorbidity. However, although cross-sectional studies cannot determine whether the associations between anxiety and multimorbidity patterns are causal, we observed that a higher prevalence of anxiety was associated with a higher number of physical co-morbidities. Longitudinal trajectories may however illuminate in more detail the likely multifactorial mechanisms underlying these cross-sectional associations. It is for example also possible that anxiety precedes the development of chronic conditions and multimorbidity. A second limitation is that the anxiety variable used was based on a single question. However, this question has been used in previous WHS publications to define anxiety [28, 29]. The assessment of the degree anxiety symptoms may have been enhanced by our use of severe and extreme categories. However, the specificity and sensitivity of this question against the gold standard diagnosis of anxiety disorders is not established. Therefore, future studies should include a more complete anxiety assessment and ideally use a clinical diagnosis. Third, since the information on chronic conditions was based on self-report, reporting biases may exist. More in detail, the reliance on self-report and not medical records may mean our data are actually underestimates. Despite these limitations, the strengths of the study include the large sample size and the multi-national scope, including most regions of the world, but in particular understudied LMICs in Africa, Latin-America, Asia and Eastern Europe.

In conclusion, our study clearly shows that the prevalence of anxiety increases with increasing numbers of comorbid chronic physical conditions. We recommend that mental health and primary care providers consider screening for the presence of anxiety symptoms especially in individuals with multimorbidity.

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Disclosures

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Table 1 Characteristics of the study sample (overall and by the presence of anxiety)

				Anxiety			
Characteristics		N	Overall	N	No	N	Yes
Sex	Male	78,783	49.4	72,661	50.7	5,412	37.7
	Female	95,806	50.6	84,714	49.3	10,339	62.3
Age (years)	18-34	73,627	47.5	68,094	49.0	4,878	34.3
	35-59	72,791	39.2	65,406	38.5	6,806	44.5
	60+	28,084	13.4	23,803	12.5	4,062	21.2
Wealth	Poorest	39,654	20.1	34,403	19.5	4,566	25.4
	Poorer	34,638	20.0	30,584	19.7	3,356	22.2
	Middle	31,673	19.9	28,419	20.0	2,620	18.7
	Richer	30,243	20.0	27,366	20.2	2,293	18.2
	Richest	29,111	20.0	26,508	20.5	1,843	15.5
Depression	No	158,015	93.0	146,570	95.5	10,853	70.3
	Yes	10,236	7.0	6,145	4.5	4,062	29.7
Angina	No	146,482	84.9	135,156	86.6	10,774	69.3
	Yes	26,035	15.1	21,123	13.4	4,821	30.7
Arthritis	No	146,192	86.2	134,272	87.4	11,364	76.1
	Yes	25,021	13.8	20,859	12.6	4,061	23.9
Asthma	No	162,998	94.5	148,371	95.2	14,028	89.0
	Yes	8,645	5.5	7,130	4.8	1,482	11.0
Chronic back pain	No	160,233	93.1	146,879	94.5	12,748	80.9
	Yes	9,985	6.9	7,336	5.5	2,626	19.1
Diabetes	No	165,074	97.0	150,161	97.4	14,309	93.0
	Yes	5,224	3.0	4,251	2.6	948	7.0
Edentulism	No	152,893	94.0	138,942	94.5	13,423	89.7
	Yes	11,119	6.0	9,487	5.5	1,587	10.3
Hearing problem	No	165,869	96.5	150,836	96.9	14,388	93.3
	Yes	6,159	3.5	4,943	3.1	1,175	6.7
Tuberculosis	No	155,773	98.3	141,893	98.6	13,276	96.0
	Yes	2,620	1.7	2,058	1.4	550	4.0
Visual impairment	No	164,051	98.6	149,276	99.1	14,377	94.2
	Yes	1,942	1.4	1,212	0.9	724	5.8
Number of chronic	0	107,183	64.4	101,135	67.3	5,701	37.8
physical conditions	1	38,258	22.1	33,555	21.2	4,586	30.1
	2	14,913	8.8	12,176	7.8	2,690	17.6
	3	5,364	3.3	4,039	2.6	1,312	9.1
	4	1,638	1.1	1,120	0.8	513	3.8
	5+	543	0.4	305	0.2	234	1.6

Data are unweighted N and weighted percentage.
The difference in sample characteristics between those with and without anxiety was statistically significant for all characteristics (Chi-squared test $p<0.001$).

Table 2 Tetrachoric correlations of physical health conditions among those with anxiety

	Angina	Arthritis	Asthma	Chronic back pain	Diabetes	Edentulism	Hearing problem	Tuberculosis	Visual impairment
Angina	1								
Arthritis	0.30*	1							
Asthma	0.24*	0.19*	1						
Chronic back pain	0.17*	0.30*	0.14*	1					
Diabetes	0.24*	0.23*	0.21*	0.18*	1				
Edentulism	0.13*	0.19*	0.17*	0.14*	0.28*	1			
Hearing problem	0.16*	0.25*	0.14*	0.17*	0.14*	0.40*	1		
Tuberculosis	0.25*	0.19*	0.30*	0.11*	0.12*	0.03	0.09*	1	
Visual impairment	0.09*	0.22*	0.16*	0.17*	0.17*	0.20*	0.38*	-0.02	1

* $p<0.05$

Table 3 Associations between chronic physical conditions and number of chronic physical conditions and anxiety estimated by multivariable logistic regression

	Model 1		**Model 2**	
	OR	95%CI	OR	95%CI
Angina	2.35**	[2.16,2.54]	1.97**	[1.79,2.16]
Arthritis	1.74**	[1.59,1.90]	1.54**	[1.39,1.70]
Asthma	1.78**	[1.57,2.02]	1.56**	[1.36,1.79]
Chronic back pain	2.67**	[2.41,2.97]	2.23**	[1.99,2.50]
Diabetes	1.99**	[1.69,2.34]	1.83**	[1.50,2.22]
Edentulism	1.14*	[1.01,1.29]	1.13	[0.97,1.31]
Hearing problem	1.63**	[1.42,1.87]	1.50**	[1.29,1.74]
Tuberculosis	2.29**	[1.84,2.84]	1.85**	[1.45,2.35]
Visual impairment	4.12**	[3.36,5.04]	3.69**	[2.95,4.62]
Number of chronic physical conditions				
0	1.00		1.00	
1	2.08**	[1.90,2.27]	1.94**	[1.76,2.13]
2	3.10**	[2.79,3.45]	2.63**	[2.34,2.96]
3	4.54**	[3.90,5.30]	3.56**	[3.00,4.22]
4	6.79**	[5.44,8.47]	4.69**	[3.64,6.04]
5+	9.66**	[6.88,13.57]	5.49**	[3.73,8.09]

Abbreviation: OR odds ratio; CI confidence interval

Each chronic physical condition or number of chronic physical conditions was included separately in different models.

Model 1: Adjusted for sex, age, wealth, and country.

Model 2: Adjusted for sex, age, wealth, depression, and country.

* $p<0.05$, ** $p<0.001$

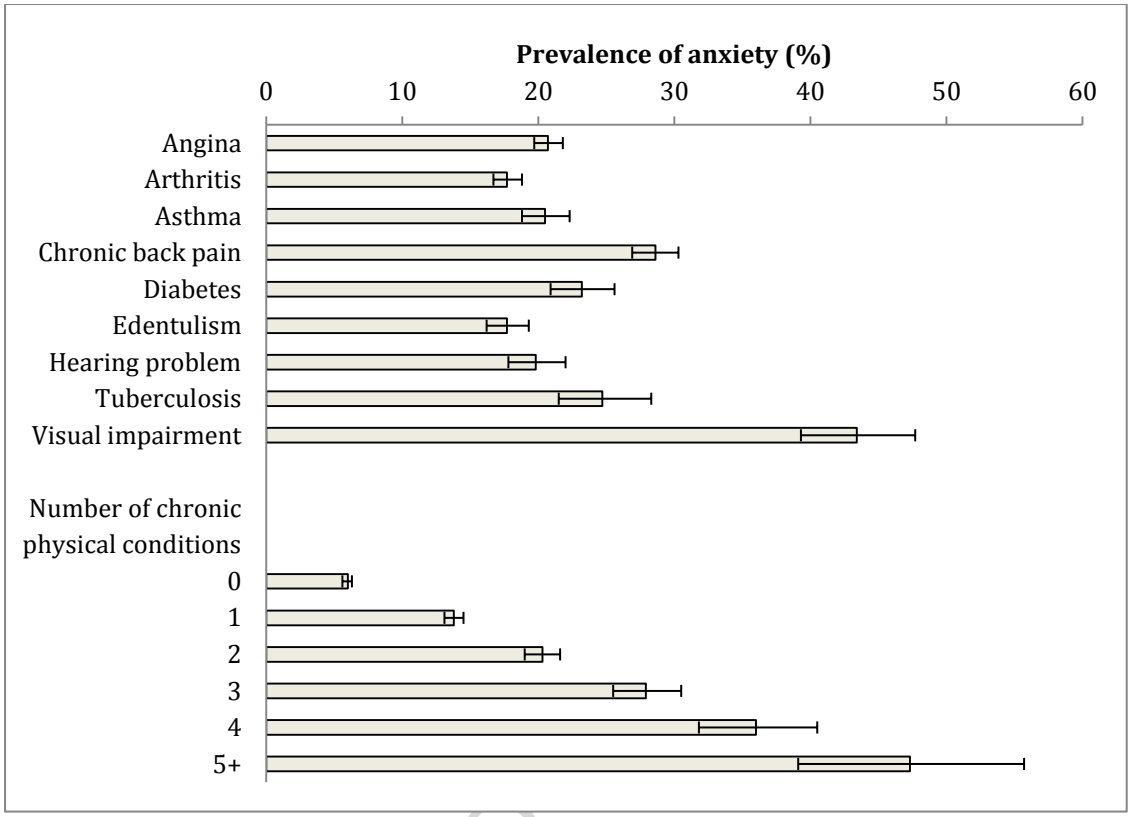

Figure 1 Prevalence of anxiety by chronic physical condition and number of chronic physical conditions

Estimates are based on weighted sample.
Bars denote 95% confidence intervals.

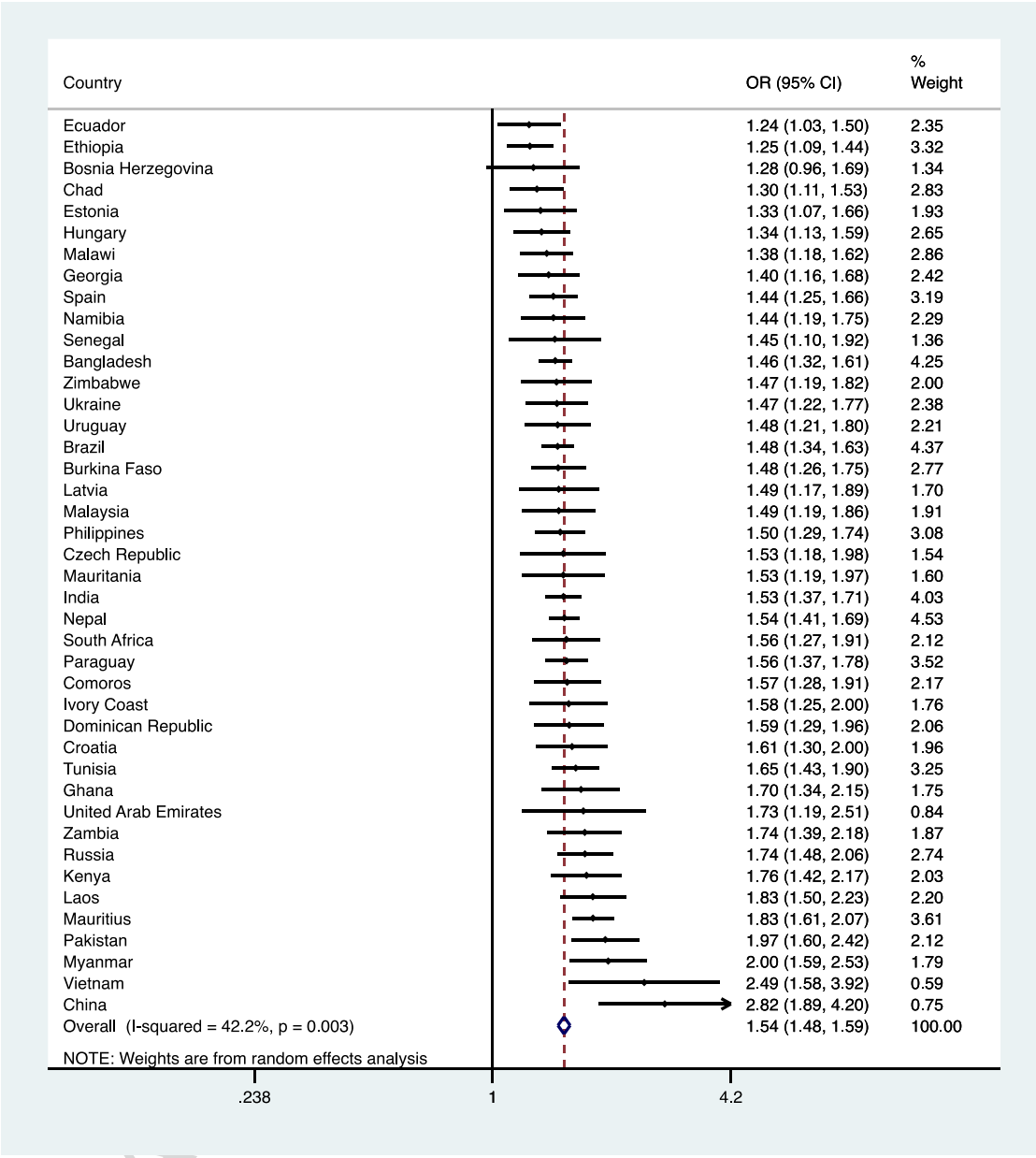

Figure 2 Country-wise association between the number of chronic physical conditions (exposure) and anxiety (outcome) estimated by multivariable logistic regression

Abbreviation: OR odds ratio; CI confidence interval
The variable on chronic physical conditions referred to the number of chronic physical conditions and was a continuous variable with values, 0, 1, 2, 3, 4, and 5+.
The models were adjusted for sex, age, wealth, and depression.